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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/583,860	05/21/2007	Takashi Nishimura	3691-0133PUS1	8593

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EXAMINER	
CHEN, SHIN LIN	

ART UNIT	PAPER NUMBER
1632	

NOTIFICATION DATE	DELIVERY MODE
03/19/2012	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

mailroom@bskb.com

Office Action Summary	Application No.	Applicant(s)	
	10/583,860	NISHIMURA ET AL.	
	Examiner	Art Unit	
	SHIN LIN CHEN	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 February 2012*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on _____; the restriction requirement and election have been incorporated into this action.

4)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

5)☒ Claim(s) *1,5-9 and 13-22* is/are pending in the application.

5a) Of the above claim(s) *6,14 and 18-21* is/are withdrawn from consideration.

6)☐ Claim(s) _____ is/are allowed.

7)☒ Claim(s) *1,5,7-9,13,15-17 and 22* is/are rejected.

8)☐ Claim(s) _____ is/are objected to.

9)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

10)☐ The specification is objected to by the Examiner.

11)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

12)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendment filed 2-7-12 has been entered. Claims 7 and 15 have been amended. Claims 1, 5-9 and 13-22 are pending. Claims 1, 5, 7-9, 13, 15-17 and 22, and the species WT1 are under consideration.

Claim Rejections - 35 USC § 102

1. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

2. Claims 1, 5, 7-9, 13, 15-17 and 22 remain rejected under 35 U.S.C. 102(a) as being anticipated by Morgan et al., September 2003 (The Journal of Immunology, Vol. 171, p. 3287-3295) and is repeated for the reasons set forth in the preceding Official action mailed 10-7-11. Applicant's arguments filed 2-7-12 have been fully considered but they are not persuasive.

Applicant cite figure of CD4+ cells and CD8+ cells and argues that CD4+ cell is not the same as a Th1 cell and Tc1 cell is completely different from a helper cell. CD4+/CD8- cells include Th0, Th1, Th2, Treg and other types of cells. The claimed methods comprise introducing a class-I restricted TCR gene into isolated helper T1 cells, which are not peripheral blood cells (amendment, p. 6-9). This is not found persuasive because of the reasons set forth in the preceding Official action mailed 10-7-11.

Morgan teaches "high efficiency TCR gene transfer into primary human lymphocytes affords avid recognition of melanoma tumor antigen glycoprotein 100" (e.g. title). Morgan shows the ability of this anti-gp100 TCR gene to transfer high avidity Ag recognition to engineered lymphocytes was confirmed in comparison with highly avid antimelanoma lymphocytes by the high levels of cytokine production (>200,000 pg/ml IFN-gamma), by recognition of low levels of peptide (<200 pM), and by HLA class I-restricted recognition and lysis of melanoma tumor cell lines. The CD4+CD8- T cells have antitumor activity and produce IFN-gamma. The Figure submitted shows that Th1 cells have antitumor effects and can produce IFN-gamma, Th2 cells do not have antitumor effect and cannot produce INF-gamma, and Treg cells suppress the antitumor effect (see amendment, p. 8). It is apparent that the CD4+CD8- cells produced by Morgan are NOT Th2 cells or Treg cells. Th0 cells are naïve T cells that are unlike activated T cells and they have not encountered their cognate antigen within the periphery. Since the CD4+CD8- T cells have antitumor activity and produce IFN-gamma, they are not likely to be Th0 cells. Further, the claims do NOT specify what type of Th1 cells are imparted antigen specificity. Therefore, the CD4+CD8- cells produced by Morgan can be considered as Th1 cells.

The claims do not specify the order of the steps, the step of "imparting antigen specificity to the helper T1 cells can be considered as first step and the step of "inducing helper T1 cells that have a nonspecific antitumor activity isolated from leukocytes isolated from a patient" can be considered as second step. The helper T1 cells are NOT necessarily isolated when they are transduced with a MHC class I-restricted T cell receptor gene. The step of "inducing helper T1 cells that have a nonspecific antitumor activity isolated from leukocytes isolated from a patient" is a general statement to "induce" helper T1 cells. The primary human lymphocytes or

peripheral blood lymphocytes basically comprise T cells, natural killer cells and B cells, and they are separated from other leukocytes. Activation of the peripheral blood lymphocytes or specifically CD4+CD8- cells with antigen specificity disclosed by Morgan can be considered as "inducing helper T1 cells that have a nonspecific antitumor activity isolated from leukocytes isolated from a patient". Thus, the claims are anticipated by Morgan.

3. Claims 1, 5, 7, 9, 13, 15, 17 and 22 remain rejected under 35 U.S.C. 102(b) as being anticipated by Clay et al., 1999 (The Journal of Immunology, Vol. 163, p. 507-513) and is repeated for the reasons set forth in the preceding Official action mailed 10-7-11. Applicant's arguments filed 2-7-12 have been fully considered but they are not persuasive.

Applicant has the same arguments as set forth above under Morgan rejection. This is not found persuasive because of the reasons set forth in the preceding Official action mailed 10-7-11 and the reasons set forth above. The CD4+ clones secret IFN-gamma and they have antitumor activity.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various

claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

6. Claims 1, 7-9, 15 and 16 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Clay et al., 1999 (The Journal of Immunology, Vol. 163, p. 507-513) in view of Bell et al., 2003 (US Patent No. 6,610,542 B1) and is repeated for the reasons set forth in the preceding Official action mailed 10-7-11. Applicant's arguments filed 2-7-12 have been fully considered but they are not persuasive.

Applicant argues that Clay fails to teach or suggest all of the elements of the instant claims, in particular, Clays fails to teach isolated helper T1 cells. Bell fails to remedy the deficiencies of Clay. Applicant cites the submitted Figure and argues that peripheral blood cells contain different immune cells and complex interactions will occur among the immune cells to be transformed. The complex interactions may lead to difficulty in controlling the reactivity of the cells involved in the immune therapy of cancer. Applicant cites Morgan et al., 2006 and Ray et al., 2010 where Steven Rosenberg is co-author for both references. Applicant argues that the approach to cancer therapy has changed from one involving immune cells of peripheral blood as disclosed in Morgan and Clay to a new approach involving isolated helper T1 cells as disclosed by the instant application (amendment, p. 9-10). This is not found persuasive because of the reasons set forth in the preceding Official action mailed 10-7-11 and the reasons set forth above under 35 U.S.C. 102.

There is no evidence of record that shows the complex interaction among different immune cells would lead to difficulty in controlling the reactivity of the cells involved in the immune therapy. The claims read on a process of preparing cells for cell therapy. Morgan and Clay show activation of CD4+CD8- cells and CD4+ cells, respectively, with antigen specificity and those cells can secret IFN-gamma and have antitumor activity, which are the properties of Th1 cells, therefore, there would be NO difficulty to **prepare** cells for cell therapy. As discussed above, the CD4+ clones taught by Clay secret IFN-gamma and they have antitumor activity. The Figure submitted shows that Th1 cells have antitumor effects and can produce IFN-gamma, Th2 cells do not have antitumor effect and cannot produce INF-gamma, and Treg cells suppress the antitumor effect (see amendment, p. 8). It is apparent that the CD4+ cells produced by Clay are NOT Th2 cells or Treg cells. Th0 cells are naïve T cells that are unlike activated T cells and they have not encountered their cognate antigen within the periphery. Since the CD4+ T cells have antitumor activity and produce IFN-gamma, they are not likely to be Th0 cells. Further, the claims do NOT specify what type of Th1 cells are imparted antigen specificity. Therefore, the CD4+ cells produced by Clay can be considered as Th1 cells. Morgan and Clay have already taught the concept of producing isolated and activated Th1 cells with imparted antigen specificity. Thus, the claims remain rejected for the reasons of record.

Conclusion

No claim is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shin-Lin Chen whose telephone number is (571) 272-0726. The examiner can normally be reached on Monday to Friday from 9:30 am to 6 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached on (571) 272-4517. The fax phone number for this group is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

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